EXHIBIT 1

Genetics Home Reference
Your Guide to Understanding Genetic Conditions
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Peters anomaly

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What is Peters anomaly?

Peters anomaly is characterized by eye problems that occur in an area at the front part of the eye known as the anterior segment. The anterior segment consists of structures including the lens, the colored part (iris) of the eye, and the clear covering of the eye (cornea). During development of the eye, the elements of the anterior segment form separate structures. However, in Peters anomaly, development of the anterior segment is abnormal, leading to incomplete separation of the cornea from the iris or the lens. As a result, the cornea is cloudy (opaque), which causes blurred vision. The opaque area (opacity) of the cornea varies in size and intensity from a small, faint streak to a large, white cloudy area that covers the front surface of the eye. Additionally, the location of the opacity varies; the cloudiness may be at the center of the cornea or off-center. Large, centrally located opacities tend to cause poorer vision than smaller, off-center ones.

Nearly half of the individuals affected with Peters anomaly have low vision early in life and about a quarter are legally blind. Due to a lack of visual stimulation, some individuals develop "lazy eye" (amblyopia). Peters anomaly is often associated with other eye problems, such as increased pressure within the eye (glaucoma), clouding of the lens (cataract), and unusually small eyeballs (microphthalmia). In most cases, Peters anomaly is bilateral, which means that it affects both eyes, although the level of vision impairment may be different in each eye. These individuals may have eyes that do not point in the same direction (strabismus). In some people with Peters anomaly, corneal clouding improves over time leading to improved vision.

There are two types of Peters anomaly, which are distinguished by their signs and symptoms. Peters anomaly type I is characterized by an incomplete separation of the cornea and iris and mild to moderate corneal opacity. Type II is characterized by an incomplete separation of the cornea and lens and severe corneal opacity that may involve the entire cornea.

How common is Peters anomaly?

The exact prevalence of Peters anomaly is unknown. This condition is one of a group of disorders known as congenital corneal opacities, which affect 3 to 6 individuals per 100,000.

What genes are related to Peters anomaly?

Mutations in the *FOXC1*, *PAX6*, *PITX2*, or *CYP1B1* gene can cause Peters anomaly. The *FOXC1*, *PAX6*, and *PITX2* genes are all members of a family called homeobox genes that direct the formation of many parts of the body. These three genes are involved in the development of the anterior segment of the eye. The *CYP1B1* gene provides instructions for making an enzyme that is active in many tissues, including the eye. The enzyme's role in these tissues is unclear; it is likely involved in the development of the anterior segment.

Mutations in any of these four genes disrupt development of the anterior segment of the eye. These mutations can lead to severe developmental problems, such as incomplete separation of eye structures and complete corneal opacity, or they can result in minor eye abnormalities including small, faint opacities. It is likely that mutations that cause a complete absence of protein function result in the most severe eye problems. It is unknown why both eyes are affected in some cases and in others only one eye is abnormal.

In many cases of Peters anomaly, there is no mutation identified in any of these four genes. The cause of the condition in these cases is unknown.

Related Gene(s)

Changes in these genes are associated with Peters anomaly.

- CYP1B1
- FOXC1
- PAX6
- PITX2

How do people inherit Peters anomaly?

Most cases of Peters anomaly are sporadic, which means that they occur in people with no apparent history of the disorder in their family. In many of these sporadic cases the genetic cause of the condition is unknown. However, some of these cases are caused by a new mutation in one of the previously mentioned genes or by the inheritance of a mutation from unaffected parents. In rare cases, the condition (or related eye disorders) has been reported to occur in multiple members of the same family.

Whether sporadic or inherited, when Peters anomaly is caused by mutations in the *CYP1B1* gene, it follows an autosomal recessive pattern of inheritance. Autosomal recessive inheritance means both copies of the gene in each cell have mutations. The parents of an individual with an autosomal recessive condition each carry one copy of the mutated gene, but they typically do not show signs and symptoms of the condition. When caused by mutations in the *FOXC1*, *PAX6*, or *PITX2* gene, the condition follows an autosomal dominant pattern of inheritance, which means one copy of the altered gene in each cell is sufficient to cause the disorder.

Where can I find information about diagnosis or management of Peters anomaly?

These resources address the diagnosis or management of Peters anomaly and may include treatment providers.

- Genetic Testing Registry: Irido-corneo-trabecular dysgenesis (http://www.ncbi.nlm.nih.gov/gtr/conditions/C0344559)

You might also find information on the diagnosis or management of Peters anomaly in Educational resources (http://ghr.nlm.nih.gov/condition/peters-anomaly/show/Educational+resources) and Patient support (http://ghr.nlm.nih.gov/condition/peters-anomaly/show/Patient+support).

General information about the diagnosis (http://ghr.nlm.nih.gov/handbook/consult/diagnosis) and management (http://ghr.nlm.nih.gov/handbook/consult/treatment) of genetic conditions is available in the Handbook. Read more about genetic testing (http://ghr.nlm.nih.gov/handbook/testing), particularly the difference between clinical tests and research tests (http://ghr.nlm.nih.gov/handbook/testing/researchtesting).

To locate a healthcare provider, see How can I find a genetics professional in my area? (http://ghr.nlm.nih.gov/handbook/consult/findingprofessional) in the Handbook.

Where can I find additional information about Peters anomaly?

You may find the following resources about Peters anomaly helpful. These materials are written for the general public.

- **MedlinePlus - Health information**
  - Encyclopedia: Cloudy Cornea (http://www.nlm.nih.gov/medlineplus/ency/article/003317.htm)
  - Health Topic: Corneal Disorders (http://www.nlm.nih.gov/medlineplus/cornealdisorders.html)
- Genetic and Rare Diseases Information Center - Information about genetic conditions and rare diseases (http://rarediseases.info.nih.gov/gard/7377/peters-anomaly/resources/1)
- Additional NIH Resources - National Institutes of Health
  National Eye Institute: Facts About the Cornea and Corneal Disease (https://www.nei.nih.gov/health/cornealdisease/)
- **Educational resources - Information pages**
  - Disease InfoSearch: Irido-corneo-trabecular dysgenesis (http://www.diseaseinfosearch.org/Irido-corneo-trabecular+dysgenesis/8682)
  - MalaCards: peters anomaly - cataract (http://www.malacards.org/card/peters_anomaly_cataract)
  - Merck Manual for Patients and Caregivers: Structure and Function of the Eyes (http://www.merckmanuals.com/home/eye_disorders/biology_of_the_eyes/structure_and_function_of_the_eyes.html)
  - Orphanet: Peters anomaly (http://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=708)
  - Scottish Sensory Centre (http://www.ssc.education.ed.ac.uk/resources/vi&multi/eyeconds/PetAno.html)
  - Seattle Children's Hospital: Eyes (http://www.seattlechildrens.org/content.aspx?id=1244)
  - The University of Arizona: Hereditary Ocular Disease (http://disorders.eyes.arizona.edu/handouts/peters-anomaly)
- **Patient support - For patients and families**
  - Children's Eye Foundation (http://childrenseyefoundation.org/meet-little-ambassadors/peters-anomaly-in-children/)
  - Contact a Family (http://www.cafamily.org.uk/medical-information/conditions/p/peters-anomalypeters-plus-syndrome/)
  - Lighthouse International: How the Eye Works (http://www.lighthouse.org/eye-health/the-basics-of-the-eye/how-the-eye-works/)
  - Resource List from the University of Kansas Medical Center: Blind/Visual Impairment (http://www.kumc.edu/gec/support/visual.html)

You may also be interested in these resources, which are designed for healthcare professionals and researchers.

- **Genetic Testing Registry - Repository of genetic test information**

    - Genetic Testing Registry: Irido-corneo-trabecular dysgenesis (http://www.ncbi.nlm.nih.gov/gtr/conditions/C0344559)
- ClinicalTrials.gov - Linking patients to medical research (https://clinicaltrials.gov/ct2/results?cond=%22Peters%20anomaly%22%20OR%20%22irido-corneo-trabecular%20dysgenesis%22)
- PubMed - Recent literature (http://www.ncbi.nlm.nih.gov/pubmed?term=%28%28peters%20anomaly%5BTIAB%5D%29%20OR%20%28irido-corneo-trabecular%20dysgenesis%5BTIAB%5D%29%29%20AND%20english%5Bla%5D%20AND%20human%5Bmh%5D%20AND%20%22last%203600%20days%22%5Bdp%5D)
- OMIM - Genetic disorder catalog (http://omim.org/entry/604229)

What other names do people use for Peters anomaly?

- irido-corneo-trabecular dysgenesis
- Peters congenital glaucoma

For more information about naming genetic conditions, see the Genetics Home Reference Condition Naming Guidelines (http://ghr.nlm.nih.gov/ConditionNameGuide) and How are genetic conditions and genes named? (http://ghr.nlm.nih.gov/handbook/mutationsanddisorders/naming) in the Handbook.

What if I still have specific questions about Peters anomaly?

Ask the Genetic and Rare Diseases Information Center (http://rarediseases.info.nih.gov/gard).

What glossary definitions help with understanding Peters anomaly?

amblyopia ; anterior ; autosomal ; autosomal dominant ; autosomal recessive ; bilateral ; cataract ; cell ; congenital ; cornea ; corneal opacity ; Descemet membrane ; dysgenesis ; enzyme ; gene ; glaucoma ; homeobox ; inheritance ; inherited ; lazy eye ; mutation ; new mutation ; opaque ; pattern of inheritance ; prevalence ; protein ; recessive ; sporadic ; strabismus

You may find definitions for these and many other terms in the Genetics Home Reference Glossary (http://ghr.nlm.nih.gov/glossary).

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For selection criteria for web links, see Genetics Home Reference at http://ghr.nlm.nih.gov/